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QUANTIFICATION OF CHIRALITY: ATTEMPTING THE IMPOSSIBLE*

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Abstract: *Contributions of A. Rassat and others to the attempt to quantify chirality are reviewed, and the limitations imposed on this endeavour by chiral connectedness, distinctions between chirality and handedness, and the non-uniqueness of chirality measures, are illustrated. Schemes for assigning absolute configuration of simple geometric objects and of objects defined by embedded graphs are outlined*

Keywords: chirality, handedness, Hausdorff distance, rotational strengths, fullerenes.

1. INTRODUCTION

This article is based mainly on the contributions of André Rassat to the discussion of chirality in chemistry, and in particular to the vexed question of its quantification. Chemists have contributed from the early days of the subject to the recognition of the

* Dedicated to the memory of André Rassat (1931-2005). This paper is based on the talk 'André Rassat, Fullerenes and Chirality' given at the Journée Scientifique en mémoire d'André Rassat, held at the Ecole Normale Supérieure, Paris, 3 May 2006.

phenomena associated with chirality (Mason, 1982) and, for obvious reasons connected to the universal occurrence of chiral molecules and selectivities in Nature, they remain interested in this topic from practical, mathematical and philosophical points of view. Apart from the very practical issue of the experimental identification of chirality, some of the many natural questions for chemists include: 'How chiral' is a given object? Is chirality different from handedness? How do we specify the absolute configuration of a chiral object? Rassat made contributions to all these questions, some aspects of which are now briefly reviewed. The history of attempts to devise measures of chirality and symmetry has recently been reviewed comprehensively by Petitjean (2003), who gives references to the contributions of many others in this well-worked field.

2. HOW CHIRAL?

When confronted with a series of chiral and achiral molecular models or other macroscopic objects, it is easy enough to separate the achiral from the chiral by eye, and it is tempting then to wonder if the set of chiral objects could also be ranked internally by their 'amount' of chirality (Figure 1).

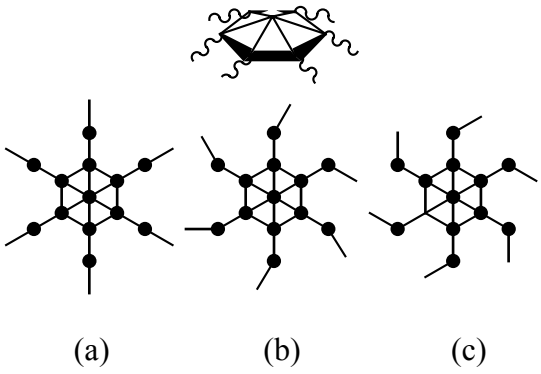

Figure 1: Geometries of a bug-shaped molecule (top) which we might hope to rank as (a) achiral, (b) chiral, (c) `more' chiral.

Given that there are left and right versions of each chiral structure, we might hope to define two types of function to measure chirality. A *degree of chirality* would be a scalar function Ψ that vanishes if and only if the object is achiral, and takes equal values for an object and its mirror image: $\Psi(R) = \Psi(L)$. A *chirality index* would be a pseudoscalar function χ that vanishes if and only if the object is achiral, and takes equal and opposite values for an object and its mirror image: $\chi(R) = -\chi(L)$. There is some

variation in terminology between, and even within, the works of various authors, with 'content', 'degree', 'index' and 'measure' all being used, sometimes in both senses.

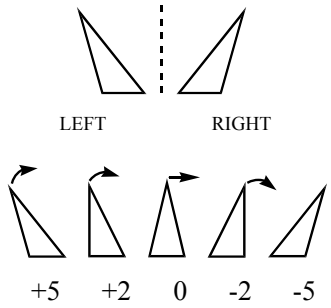

Figure 2: Series of triangles interpolating smoothly between 2D-left and 2D-right forms, with a notional chirality index value at each stage.

The triangle in the two-dimensional world of 'Flatland' (Abbott, 1884/1978) is an object for which both types of function can be defined (Figure 2), but as soon as we move to more complex objects, a problem becomes apparent. Any continuous motion within the 'shape-space' of all triangles that interconverts the 2D-left and 2D-right forms must at some point pass through an achiral configuration, where the necessary switch in sign of the chirality index can occur by passing through zero. In contrast, even the relatively simple shape shown in Figure 3 can be converted from left to right forms without ever passing through an achiral configuration.

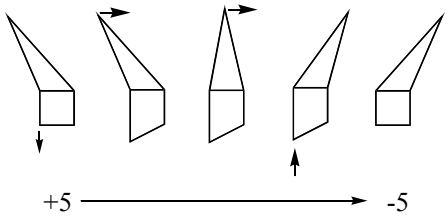

Figure 3: An illustration of chiral connectedness: a series of hat-shaped objects interpolating smoothly between 2D-left and 2D-right forms, without ever passing though a 2D-achiral configuration.

This is an illustration of *chiral connectedness* (Mezey, 1995; Weinberg and Mislow, 1997) Two enantiomeric objects are chirally connected if there is some continuous path between them that passes though only chiral configurations. The problem for definition of a continuous function that is to serve as a chirality index is then clear: the function must pass from $\chi(L)$ to $\chi(R) = -\chi(L)$ via a zero that applies in some chiral configuration. Thus, every pseudoscalar chirality index must have a 'false zero' (Ruch,

1972; Buda *et al*., 1992; Harris *et al*., 1999) somewhere: there must be at least one chiral object with $\chi(R) = -\chi(L) = 0$ for any particular definition of χ. Some authors call such objects *non-handed*, and say that they possess only *latent*-handedness (Pinto and Avnir, 2001). In fact, essentially all of the objects in 2D or 3D that are sufficiently complicated to be of interest are also chirally connected, and so the initially attractive idea of a *continuous* chirality index has in general to be abandoned. Even an object as simple as the (unlabelled) tetrahedron is chirally connected, as is the unlabelled simplex in any number of dimensions greater than two (Weinberg and Mislow, 1997).

At least in the 2D universe of triangles, there is the possibility of defining a chirality index, and so it is possible to ask if one triangle is 'more (2D)chiral' than another. Many papers have discussed the question of the 'most (2D)chiral' triangle (see, for example, long lists in (Petitjean, 2003; Rassat and Fowler, 2003)), and have come to different conclusions about its identity, some quite bizarre in that the most chiral triangle is 'flat', with one 0º or 180º angle. A conjecture was hazarded that there existed some valid measure that would make any scalene triangle 'the most chiral triangle' (Dunitz, 2000). A systematic treatment solved this problem and gave a simple direct proof that the conjecture was correct (Rassat and Fowler, 2003).

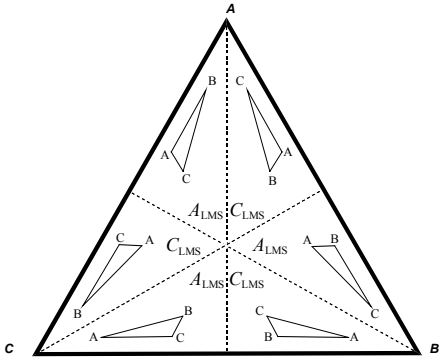

Figure 4: Triangular shape-space diagram. Each vertex of a semi-regular hexagon of points on the diagram represents a permutation of vertex labels of a given physical triangle ABC and its enantiomer in the shape space defined by reduced angles. The six compartments are labelled by the order of the angles and, with the convention that the vertex labels ABC run clockwise, alternate compartments contain the physical triangle and its enantiomer. A 2D-chirality descriptor C_{LMS}/A_{LMS} can be assigned to the 2D-enantiomers.

The argument relies on a simple representation of the shape space of triangles (Figure 4). Up to similarity, a triangle ABC is specified by two independent parameters which can be taken to be the reduced internal angles, $a\pi$, $b\pi$, $c\pi$ with $a + b + c = 1$. A convenient and symmetrical way of representing three quantities that sum to a constant is through the triangular diagram traditionally used to present the thermodynamic phase

properties of ternary mixtures. Every scalene triangle is represented six times in the full diagram, once in each right-angled 'fundamental region'.

Absence of chiral connectedness is apparent from the fact that all paths from one fundamental region to another pass through median lines representing achiral configurations. To keep track of the redundancies in the representation, an *ad hoc* descriptor, say C_{LMS} or A_{LMS}, can be assigned to the two enantiomers, according to whether the **L**arge **M**edium and **S**mall angles run in *C*lockwise or *A*nticlockwise order.

In this representation, a chirality index is a continuous function of the shape, invariant under similarity and normalisable, that vanishes on the edges and median lines of the diagram, and only there. Such a function has A_2 symmetry in the C_{3v} point-group symmetry of the diagram – with alternating positive and negative lobes as we cycle through the six fundamental regions. It is desirable that the function have a single maximum in each positive lobe, but that is not forced by the defining conditions (Buda *et al*., 1992; Osipov *et al*., 1995; Weinhold and Mislow, 2000). There are infinitely many acceptable functions, including the lowest A_2 wavefunction for the Schrödinger equation of the particle in an equilateral triangular box (Bhattacharjee and Banerjee, 1987), a modified Guye function $abc(a\text{-}b)(b\text{-}c)(c\text{-}a)$, the Dunitz sine function $(\sin \pi a - \sin \pi b)(\sin \pi b - \sin \pi c)(\sin \pi - \sin \pi a)$, and many other combinations that are equally plausible. In general, all give different locations for the maximum, and the maximum can be pushed around the compartment in shape space by multiplying the A_2 function by any A_1 function. Choice of the A_1 function as a hexagonal 'crown' of delta-function spikes, or exponential approximations to them, allows the extrema to be pushed onto the set of six points representing any particular scalene triangle, hence demonstrating the claim in the title of the 2003 paper 'Any scalene triangle is the most chiral triangle'.

An analogous argument can be constructed for chiral tetrahedra (Rassat and Fowler, 2004). The unlabelled tetrahedron is chirally connected, and so we cannot hope for a pseudoscalar chirality index. However, it is possible, by inspection of all the combinations of distinct edge lengths that can occur in a tetrahedron, to construct a scalar function that vanishes for achiral but not for chiral tetrahedra. The paper lists 25 such combinations, distributed over the allowed point group symmetries of T, D_{2d}, C_{3v}, D_2, C_{2v}, C_2, C_s, and C_1 and notes that achirality of a tetrahedral array of four points implies the presence of a mirror plane, and an edge in that plane. The trick is then to define a factor for each edge that vanishes if that edge lies in a mirror plane: if AB lies in the mirror plane, for example, take the factor $f_{AB} = (|AC| - |AD|)^2 + (|BC| - |BD|)^2$ defined in terms of edge lengths. A product of factors $f_{AB} f_{AC} f_{AD} f_{BC} f_{BD} f_{CD}$ vanishes for

any mirror-symmetric tetrahedron, and multiplication by the volume of the tetrahedron excludes 'paradoxical' (Buda *et al*., 1992) degenerate cases. As before, the argument now runs that multiplication of this basic function by totally symmetric functions can be used to push the maximum of the function to any desired point in shape space, and the search for a unique 'most chiral' tetrahedron is therefore futile. An extended Dunitz conjecture holds for tetrahedra as well as triangles, for degrees of chirality as well as indices of chirality.

3. CHIRAL AND HANDED?

Ruch (1972) famously introduced the analogy of potatoes and shoes to illustrate a distinction between two types of chiral objects that we might wish to classify. Imagine two boxes. We are given a set of chiral objects and asked to assign each object to a box. In the weak version of the assignment problem, Game 1, we must ensure that objects are assigned subject only to the condition that no two enantiomers end up in the same box. In the stronger version, Game 2, we are asked to put all 'right' enantiomers in one box (*R*) and all 'left' enantiomers in the other (*L*).

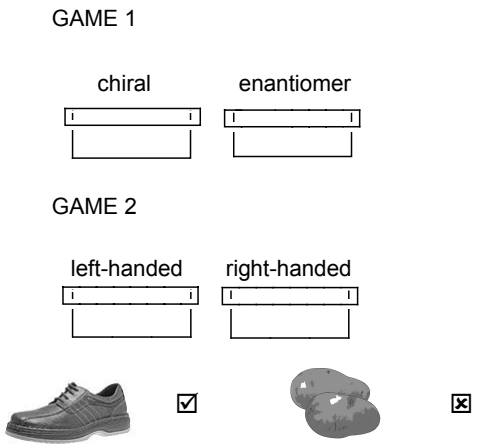

Figure 5: Two assignment games for chiral objects, and examples of easy and difficult objects.

As Ruch points out, we could expect to perform the second task easily enough for shoes, despite the many differences between two arbitrary right shoes, but not for potatoes, where we can easily see that each individual object is chiral (non-superimposable on its mirror image) but we have no obvious way of labelling it *R* or *L*. 'Any classification would be very artificial.' Ruch also notes that other objects such as

screws belong to the shoe-like category in that they too can be split into disjoint right and left forms; in this case, according to the direction of motion when the screw is turned in a clockwise sense. This observation itself raises further difficulties. Although the test proposed for the handedness of a screw is reasonable, and may appear natural to a right-handed person in a tool-using culture, there is no necessary connection between *R* and *L* shoes and *R* and *L* screws. This depends on a convention.

The distinction between the two types of objects, with shoe-like and potato-like chirality, corresponds to the difference that is drawn between chirality and handedness (King, 2003). This distinction is potentially significant in chemistry: chiral molecules have a huge variety of shapes, with no obvious correspondence to left or right shoes, and so in general they are potato-like and not handed.

However, a distinction based on a notion of what is natural is not clear-cut. For instance, one can easily imagine an innovative fashion designer, or the effects of extreme wear and tear, producing shoes that would puzzle the classifier. What about flat but chiral insoles for shoes (Figure 6), where the insert for the right shoe actually looks more like a left shoe when viewed from the marked side? (The insole is marked, on one side only, with various curves to make it easy to cut down to the correct shoe size and shape. After cutting it is to be turned over for insertion into the shoe. Is it then the look or the destination of the insole that should determine the choice of left/right label?)

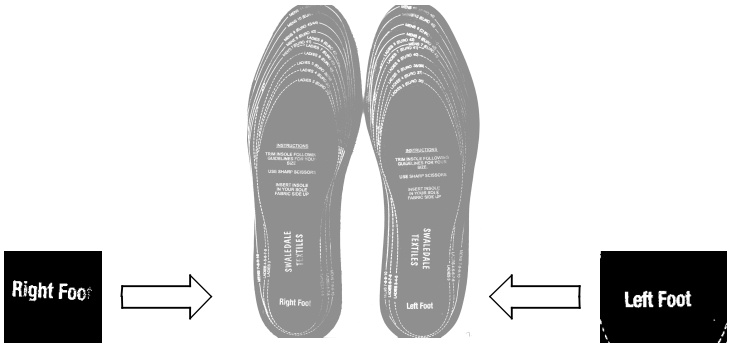

Figure 6: A pair of physically shoe-like objects (insoles, semelles intérieures) with potato-like chirality?

Similarly, it is at least conceivable that a principle accepted as 'natural' by some cohort of researchers could be derived for potatoes, perhaps based on a chiral effect reflecting the chirality of the cause, in line with Curie's Principle. In the molecular domain,

optically active molecules of any shape have long been classifiable in a ‘natural’ way, by reference to the sign of the optical rotatory power under specific conditions. At the present time, the Cahn-Ingold-Prelog (CIP) rules (1966) constitute a definition of what is considered by chemists to be natural in the molecular context, and give an algorithmic procedure for the classification problem at the level of the atoms and groups making up the molecule. These examples suggest that, given a sufficiently flexible notion of what is natural, it should be possible to attribute handedness to any class of chiral objects. Handedness may be in the eye of the beholder. Any convention is inevitably local to some class of ‘similar’ objects. Chiral connectedness also implies that, even within such a restricted class, the assigned handedness of objects may be subject to sudden jumps between arbitrarily closely related objects.

Subject to these limitations, it is still of interest to look for classification schemes that can assign handedness in particular contexts. For his last published paper on chirality (Fowler and Rassat, 2006), Rassat set up a scheme with a descriptor for right and left geometric tetrahedra which used the ordering of edge lengths around vertices, applied in the spirit of the Cahn-Ingold-Prelog RS and PM priority rules, to label all chiral tetrahedra (Figure 7). Avnir (2004) has mentioned a possible alternative scheme based on the CIP logic applied to the face of maximum perimeter, which uses less detail about the tetrahedron and, as he shows, suffers from the non-handedness difficulty.

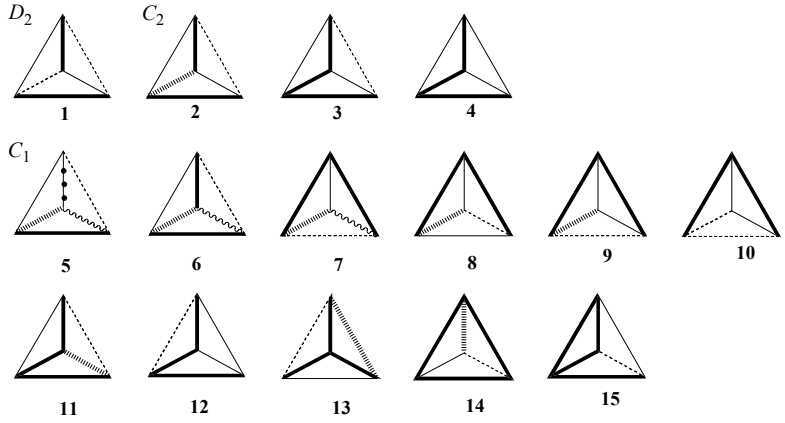

Figure 7: The fifteen edge-length claases of chiral tetrahedra. All but case **4** can be assigned an *R* or *S* label based on the ordering of edge lengths around a `senior vertex’ (Fowler and Rassat, 2006) and in case **4** the sense of the helix of three equal edges is used to assign the label.

4. HAUSDORFF DISTANCE AND HANDEDNESS

An influential paper in the area of chirality was the Comptes Rendus article (Rassat, 1984) that introduced the idea of using Hausdorff distance to assign handedness to geometrically defined molecular and other objects. Despite the well known reluctance of chemists to adopt unfamiliar mathematical ideas, this paper has received over 40 citations in the chemical literature to date. The basic idea was to assign the labels Left and Right on the basis of the distance, appropriately defined, from standard Left and Right objects. The measure of distance adopted was the set-theoretic notion of Hausdorff distance. Technically, the Hausdorff distance between two sets of points A and B with members a and b is given by the expression

$$H(A,B) = \max \{h(a , b), h(b, a)\}$$

where

$$h(a , b) = \max_a \{ \min_b \{ d(a , b)\}$$

and $d(a , b)$ is the usual Euclidean distance. $H(A,B)$ is the smallest radius d for which it is true that every point in A has a neighbour in B within distance d and every point in B has a neighbour in A within distance d. In practice, the calculation for two fixed sets of points is straightforward (Figure 8). The calculation for the purposes of assignment of Left/Right labels involves a further step, as the *minimum* Hausdorff distance between the object to be assigned and the test objects is required – so $H(A,B)$ must be minimised over all possible orientations and positions of the object to be assigned.

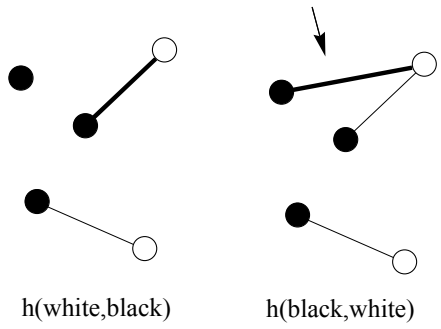

Figure 8: Scheme of calculation of a Hausdorff distance. The sets of white and black points are A and B of the definition. The distance from the white to the black set is found by taking the distance of each white point to its nearest black neighbour, then taking the such longest nearest-neighbour distance (≡ h(white,black)). The distance from the black to the white set is found by taking the distance of each black point to its nearest white neighbour, then taking the longest such nearest-neighbour distance (≡ h(black,white)). The larger of the two h values is then the Hausdorff distance H between the two sets.

The Rassat (1984) criterion is then simply: for a given object to be assigned, calculate the Hausdorff distances from it to the Left and Right reference objects, and if those distances differ, the object takes the handedness label of the nearer test object. The test objects are in principle arbitrary, but are taken to be the right-angled tetrahedra T_0 {(0,0,0), (1,0,0), (0,2,0), (0,0,3)} for Right, and its inversion partner {(0,0,0), (−1,0,0), (0,−2,0), (0,0,-3)} for Left.

Three possible outcomes of the distance test are envisaged in the original article: an object may be straightforwardly assignable as Right or Left, or the two distances may be equal, when the object is in the so-called intermediate case. Achiral objects are intermediate in this classification, but it is noted that one cannot exclude the possibility that a chiral object will be equidistant in the Hausdorff sense from both reference tetrahedra.

It is now clear that chiral connectedness implies that such unassignable objects must exist, and so the scheme cannot be universal. It becomes then a practical question to decide whether the utility of such a scheme for a restricted set of objects to be tested outweighs the objection in principle that some exceptions may be found (Buda and Mislow, 1992). That particular debate rumbles on, as other indices are regularly proposed, found useful in some context but attacked on grounds of unacceptability in principle (e.g. Osipov et al., 1995; Millar et al., 2005).

The Hausdorff distance has been used in a different way, to provide what in our terms is a degree of chirality. Buda and Mislow (1992) define such a function (in their terminology, a measure of chirality) by the minimised Hausdorff distance between an object and its enantiomer. They point out that such a function vanishes if and only if the object and its enantiomer can be made to coincide, and hence takes the value zero if and only if the object is achiral. The Hausdorff chirality measure is therefore a proper choice for a degree of chirality, though of course it has no claim to uniqueness, as the discussion of ‘most chiral objects’ in the previous session has emphasised.

Another use of distance-based quantities is based on the continuous symmetry measures (CSM) and continuous chirality measures (CCM) which are based on the idea of finding, for some given object to be tested, the nearest object of a given symmetry. In this approach, devised by Avnir and his group (Zabrodsky et al., 1992; Zabrodsky and Avnir, 1995), and applied in a long series of papers to many problems of symmetries of microscopic and macroscopic objects, the reference object is constructed, rather than given. A useful tutorial review article is the one by Alvarez et al. (2005), and many of

the relevant papers from the Jerusalem group are listed in the review by Petitjean (2003).

5. PHYSICAL HANDEDNESS OF GRAPHS?

The spectroscopic manifestations of chirality depend on the fact that enantiomeric molecules rotate the plane of polarised light oppositely, and thus an optical rotation can in principle be measured for an enantiomerically enriched or enantiomerically pure sample. A 2003 paper (Rassat *et al*., 2003) developed the physical analogy in a further approach to the question of assigning handedness to molecules, and by extension to all structures that can be represented by embeddings of cubic (in the sense of trivalent) planar graphs. The idea is to treat an embedded graph as if it were a chiral molecule, specifically a framework of carbon atoms, and to calculate its optical rotatory power from the simplest possible model of its electronic structure, Hückel theory. The sign of the rotation then gives the handedness of the molecule/graph. The calculation involves two ingredients. The chiral molecule/graph has to be embedded in space: the positions of the real or notional carbon nuclei/vertices are either given, or they are calculated from the 'topological coordinates' (Fowler and Manolopoulos, 1995). The molecular orbitals of the carbon cluster whose skeleton is the graph are then calculated by Hückel theory (Streitwieser, 1962), and used, together with the nuclear positions in a calculation of rotatory power.

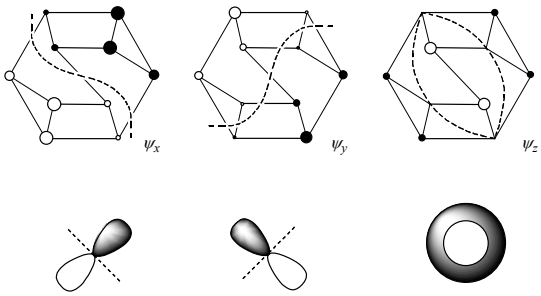

Figure 9: Schematic representation of three adjacency eigenvectors for a small spheroarene, showing the correspndence to speherical harmonic functions. If the entries of each vector are interpreted as cartesian coordinates ('topological coordinates' (Fowler and Manolopoulos, 1995)) in the directions indicated, we have a useful embedding of the graph on the sphere in 3D space.

It should be emphasised that both stages involve only a single main calculation: the diagonalisation of the adjacency matrix of the graph. The adjacency matrix **A** has entries $\mathbf{A}_{ij} = 1$ for vertices connected by an edge of the graph, and otherwise $\mathbf{A}_{ij} = 0$.

For planar graphs, an embedding, with coordinates, on the sphere can be obtained by finding three eigenvectors of **A** that mimic singly-noded spherical harmonics (Fowler and Manolopoulos, 1995).

In Hückel theory, the eigenvectors of **A** correspond to π molecular orbitals and can be assigned an electron occupation of electron based on their eigenvalue. The two eigenvectors of most interest are those of the HOMO (Highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital), which for an uncharged system correspond to the eigenvalues at positions $n/2$ and $n/2+1$ when the n eigenvalues are arranged in non-increasing order. A closed formula in terms of eigenvector coefficients and eigenvalues of the adjacency matrix is obtained for the rotational strength of each transition between occupied and unoccupied orbitals of the notional or real chiral molecular π system (See equation (12), Rassat et al., 2003). This is applied to the HOMO-LUMO pair, and the sign of the rotational strength is taken as the chirality descriptor (i.e., the handedness). If this transition fails to give a non-zero result, priority rules are followed until a pair is found that does give a non-zero contribution. The resulting descriptor gives a specification of the absolute configuration of the embedded graph/molecule.

It is theoretically possible that a chiral graph/molecule will give zero rotational strengths for all pairs, and this would correspond to the unusual experimental situation of a chiral molecule without detectable optical rotation. The likelihood of such exceptions seems *a priori* small, as it could require as many $n/2 \times n/2$ coincidental false zeroes if the point-group symmetry is trivial. The target here is a descriptor not an index, and the graph and its enantiomer are not even notionally connected by a smooth path, by the discrete nature of graphs. The topological rotational strength approach for calculating descriptors has been applied to a number of chiral fullerenes and other cubic polyhedra.

6. CONCLUSION

It may seem natural to attempt to rank chiral objects by the amount of their chirality, but the attempt is fraught with difficulties. Chiral connectedness of all but the simplest objects implies an internal contradiction in the notion of a continuous chirality index, Freedom in the definition of degree of chirality implies non-uniqueness of any putative ‘most chiral’ object. The apparently sharp distinction between potato-like chirality and shoe-like handedness becomes blurred under closer inspection. This short review has discussed some contributions of one innovative researcher worker in the field, which

illustrate the extent to which those difficulties can be avoided in specific contexts. Particular contributions of A. Rassat to the definition of absolute configuration of geometric and combinatorial objects have been highlighted.

REFERENCES

Abbott, E.A., (1884) *Flatland, A Romance of Many Dimensions*, Reprint Oxford, Basil Blackwell 1978.

Alvarez S., Alemany P. and Avnir D. (2005) Continuous chirality measures in transition metal chemistry, *Chemical Society Reviews,* 34, 313-326.

Avnir, D., Yogev-Einot, D, Katzenelson, O. and Pinto, Y. (2004) The elusive nature of handedness and homochirality, 18th ILASOL Meeting, Rehovot, Israel. (See http://www.ilasol.org.il and http://chem.ch.huji.ac.il/employee/avnir/presentations.html).

Bhattacharjee, J.K., and Banerjee, K. (1987) Ground-State Energy Of A Particle In A Polygonal Box , *Journal of Physics. A-Mathematical and General*, 20, L759-761.

Buda, A.B., Auf der Heyde, T., and Mislow, K. (1992) On Quantifying Chirality, *Angewandte Chemie International Edition in English*, 31 989-1007.

Buda, A.B., and Mislow, K. (1992) A Hausdorff Chirality Measure, *Journal of the American Chemical Society*, 114 6006-6012.

Cahn, R.S., Ingold, C.K., Prelog, V., (1966) Specification of Molecular Chirality, *Angewandte Chemie International Edition in English*, 5 (1966) 385-415.

Dunitz, J., Unpublished manuscript, sent as personal communication to A.Rassat, 11 October 2000.

Fowler, P.W. and Manolopoulos, D.E. (1995) *An Atlas of Fullerenes*, Oxford: Oxford University Press, viii+392pp; Reprint: New York: Dover Publications, 2007.

Fowler, P.W., and Rassat, A. (2006) A classification scheme for chiral tetrahedra, *Comptes Rendus Chimie* 9 1203-1208.

Harris, A.B., Kamien, R.D., and Lubensky, T.C., (1999) Molecular chirality and chiral parameters, *Reviews of Modern Physics*, 71 1745-1757.

King, R.B. (2003), Chirality and Handedness – The Ruch 'shoe-potato' dichotomy in the right-left classification problem, *Annals of the New York Academy of Sciences*, 988 158-170.

Mason, S.F., (1982) *Molecular Optical Activity and the Chiral Discriminations*, Cambridge, Cambridge University Press 288pp.

Mezey, P.G. (1995) Rules On Chiral And Achiral Molecular-Transformations, *Journal of Mathematical Chemistry*, 17 185-202.

Millar, G., Weinberg, N. and Mislow K.(2005) On the Osipov-Pickup-Dumnmur Chirality Index: Why Pseudoscalar Functions are Generally Unsuitable to Quantify Chirality, *Molecular Physics,* 103 2769-2772.

Osipov, M.A., Pickup, B.T., Dunmur, D.A. (1995) A New Twist to Molecular Chirality – Intrinsic Chirality Indexes, *Molecular Physics,* 84 1193-1206.

Petitjean, M. (2003) Chirality And Symmetry Measures: A Transdisciplinary Review, *Entropy*, 5 271-312.

Pinto, Y. and Avnir, D. (2001) A Generalized Handedness Labeling Strategy: Addressing Latent Handedness in Chiral Structures, *Enantiomer*, 6, 211–217.

Rassat, A. (1984) Criterion Derived From Hausdorff Distance For The Classification of Chiral Point Systems, *Comptes Rendus de l'Académie des Sciences Serie II,* 299 53-55.

Rassat, A., and Fowler, P.W., (2003) Any scalene triangle is the most chiral triangle, *Helvetica Chimica Acta* 86 1728-1740.

Rassat, A., and Fowler, P.W., (2004) Is there a 'most chiral tetrahedron'?, *Chemistry - A European Journal*, 10 6575-6580.

Rassat, A., László, I., and Fowler, P.W., (2003) Topological rotational strengths as chirality descriptors for fullerenes, *Chemistry - A European Journal,* 9 644-651.

Ruch, E. (1972) Algebraic Aspects of Chirality Phenomenon in Chemistry, Accounts of Chemical Research, 5 49-56.

Streitwieser, A. Jr, (1962) Molecular Orbital Theory for Organic Chemists, New York: John Wiley & Sons, viii+489pp.

Weinberg, N. and Mislow K.(1997) On Chiral Pathways in E(n): A Dimensional Analysis, *Theoretica Chimica Acta,* 95 63-65.

Weinberg, N. and Mislow K.(2000) On Chirality Measures and Chirality Properties, *Canadian Journal of Chemistry,* 78 41-45.

Zabrodsky H. and Avnir, D. (1995) Continuous Symmetry Measures, IV: Chirality, *Journal of the American Chemical Society*, 117, 462-473.

Zabrodsky, H., S. Peleg S. and Avnir, D. (1992) Continuous Symmetry Measures, *Journal of the American Chemical Society*, 114, 7843-7851.